

transgenic or chimeric or mosaic bovines. The Examiner's comments are now addressed in turn.

1. Double Patenting

Applicants agree to provide a terminal disclaimer with respect to US 5,741,957 and US 5,633,076 on notification of allowable subject matter.

2. 35 USC 112 First Paragraph

The Examiner questions whether the specification provides support for the term "chimeric bovine." Support is provided at p.32, line 20.

The Examiner says the specification lacks enablement for a chimeric bovine producing a protein in its milk. The Examiner cites a reference in which the term chimeric is used to indicate a "composite individual formed from two cells of separate origin." The Examiner says that production of such a chimeric bovine would require use of bovine embryonic stem cells, which applicants have not enabled. The Examiner notes that applicants have produced a mosaic bovine, but says that a mosaic bovine is not a chimeric bovine, this being according to one reference, an "individual with two strains of cells derived by nondisjunction or mutation after the zygote forms." However, the Examiner says that since the phenotype of a mosaic bovine results from a random mutations, the phenotype is completely unpredictable. Finally, the Examiner says that there is no evidence that either a mosaic or a chimeric bovine passes a transgene to descendants.

The distinction in usage between "mosaic" and "chimeric" in the references cited by the Examiner resides in differences in the mechanisms of production that do not necessarily result in any differences in the resulting bovines. Both "chimeric" and "mosaic" animals, in the sense these terms are used in the cited references, have some cells containing an integrated construct and others cells that lack such a construct. Thus, it is entirely reasonable to use a single generic term to describe bovines containing a construct in some cells and not others, and this is what applicants have done. Such is apparent from p. 32, lines 17-24 of the specification, in which the terms "chimeric" and "mosaic" are used synonymously in successive sentences.

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Given applicants' generic usage of the term "chimeric," it is sufficient that the specification provide one route for producing such animals, and immaterial whether other routes, such as those requiring embryonic stem cells, would also have been successful. Chimeric animals (in the generic sense this term is used by the present applicants) can in fact be produced by the same general procedure as is taught by the specification for producing transgenic animals. Whether a transgenic animal or a chimeric animal results depends on whether a transgene integrates at the one-cell stage or subsequently. As noted, at p. 90 and at p. 118, in applicants' own examples, both chimeric and transgenic animals were produced.

With respect to the alleged unpredictability of a chimeric animal expressing a protein in milk, it is submitted that a chimeric animal that is female and has integrated an appropriately designed expression construct in its mammary gland would be expected to express the construct in similar manner to a transgenic animal that has integrated the transgene in every tissue. Such a chimeric bovine can readily be identified by screening a tissue sample from the mammary gland for an incorporated construct. As with transgenic animals, it is not expected that every chimeric animal will express, or will express at high levels. Nevertheless, by screening a reasonable number of such chimeric bovines, first by detecting construct in the mammary gland, and then by screening for protein in the milk, it is reasonably expected that at least one chimeric bovine having the desired property of producing a protein in milk will be isolated.

Applicants acknowledge that chimeric bovines are not necessarily capable of germline transmission. Thus, the claims have been amended so that the reference to "descendant" applies only to a transgenic bovine.

Applicants attach copies of 35 USC 132 declarations from the parent case, as requested by the Examiner.

With respect to the Examiner's aside regarding an apparent inconsistency in the sex of a calf#15 described at p. 90 of the specification and another calf#15 described at p. 119, the Examiner is advised that the two are different animals, and the designation calf#15 for both is coincidental. Thus, there is no inconsistency.

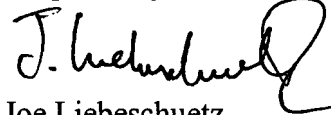
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35 USC 112, second paragraph

The Examiner says that claims 114-117 are confusing in their reference to chimeric bovines containing a transgene because transgene are by definition present in the germline. The claims have been amended to refer to a construct rather than a transgene to moot this rejection.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

Respectfully submitted,



Joe Liebeschuetz
Reg. No. 37,505

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, 8th Floor
San Francisco, California 94111-3834
Tel: (415) 576-0200
Fax: (415) 576-0300
JOL:dmv

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